

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A modified antibody of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain variable region and a heavy chain constant region wherein at least amino acid ~~residues~~ residue 250, EU numbering, is glutamic acid or glutamine and amino acid residue 428, EU numbering, is leucine or phenylalanine ~~are different from the residues present in the unmodified human class IgG antibody.~~
2. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.
3. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.
4. (Canceled)
5. (Previously presented) The modified antibody according to Claim 2, wherein said unmodified class IgG antibody is a human class IgG1 antibody.
6. (Previously presented) The modified antibody according to Claim 1, wherein the unmodified antibody is
OST577-IgG2M3, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 2, 4, and 5, respectively, or

OST577-IgG1, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 3, 4, and 5, respectively.

7. (Canceled)

8. (Currently amended) A modified antibody of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein:

~~——(a)—— amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid or glutamine; or~~

~~——(b)—— amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine or leucine.~~

9. (Previously presented) The modified antibody according to Claim 1, wherein amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine.

10. (Previously presented) The modified antibody according to Claim 1, wherein amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

11. (Previously presented) A modified antibody of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein:

(a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

12. (Previously presented) The modified antibody according to Claim 1, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

13-14. (Canceled)

15. (Currently amended) [[A]] The modified antibody according to Claim 8, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule of class IgG with FeRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein:

—— (a) —— ~~amino acid residue 250, EU numbering, from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or~~

—— (b) —— ~~amino acid residue 428, EU numbering, from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.~~

16. (Currently amended) The modified antibody according to Claim 8, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule ~~15, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is aspartic acid.~~

17. (Currently amended) The modified antibody according to Claim 15, wherein said unmodified class IgG antibody is a human class IgG1 antibody amino acid residue 428, EU numbering, from the heavy chain constant region is glycine.

18. (Original) The modified antibody according to Claim 1, wherein the modified antibody has a higher binding affinity for FcRn at pH 6.0 than at pH 7.4.

19. (Currently Amended) An antibody comprising a heavy chain variable region and a heavy chain constant region substantially identical to that of a naturally occurring class IgG antibody, wherein at least the heavy chain constant region amino acid ~~residues~~ residue 250, EU numbering, is glutamic acid or glutamine and amino acid residue 428, EU numbering, is leucine or phenylalanine ~~are different from the residues present in the naturally occurring class IgG antibody,~~ and wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

20. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.

21. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.

22. (Canceled)

23. (Previously presented) The antibody according to Claim 20 wherein said naturally occurring class IgG antibody is a human class IgG1 antibody.

24. (Currently amended) An antibody comprising a constant region substantially identical to that of a naturally occurring class IgG antibody wherein:

~~——(a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid or glutamine; or~~

~~——(b) amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine or leucine; and~~

~~wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.~~

25. (Previously presented) The antibody according to Claim 19, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine.

26. (Previously presented) The antibody according to Claim 19, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

27. (Previously presented) An antibody comprising a constant region substantially identical to that of a naturally occurring class IgG antibody wherein:

(a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and said amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine; and

wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

28. (Previously presented) The antibody according to Claim 19, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

29-30. (Canceled)

31. (Currently amended) [[An]] The antibody according to Claim 24, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule comprising a constant region substantially identical to that of a naturally occurring class IgG antibody wherein:

—— (a) —— ~~amino acid residue 250, EU numbering, from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or~~

—— (b) —— ~~amino acid residue 428, EU numbering, from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine; and~~

~~wherein the *in vivo* serum half life of said antibody is increased relative to the naturally occurring antibody.~~

32. (Currently amended) The antibody according to Claim 24, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule 31, ~~wherein said amino acid residue 250 from the heavy chain constant region is aspartic acid.~~

33. (Currently amended) The antibody according to Claim 31, wherein said unmodified class IgG antibody is a human class IgG1 antibody ~~amino acid residue 428 from the heavy chain constant region is glycine.~~

34. (Currently Amended) A modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an *in vivo* mean elimination half-life at least about 1.8-fold longer than that of the corresponding unmodified class IgG antibody and

wherein in said heavy chain constant region, residue 250, EU numbering, is glutamic acid or glutamine and residue 428, EU numbering, is leucine or phenylalanine.

35. (canceled)

36. (Currently amended) A modified antibody of class IgG with an *in vivo* mean elimination half-life at least about 1.8-fold longer than that of the corresponding unmodified class IgG antibody, wherein:

(a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

37. (Previously presented) The modified antibody of Claim 34, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

38. (canceled)

39. (Currently Amended) A modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an *in vivo* mean serum clearance rate at least about 1.8-fold lower than that of the corresponding unmodified class IgG antibody and

wherein in said heavy chain constant region, residue 250, EU numbering, is glutamic acid or glutamine and residue 428, EU numbering, is leucine or phenylalanine.

40. (canceled)

41. (Currently Amended) A modified antibody of class IgG with an *in vivo* mean serum clearance rate at least about 1.8-fold lower than that of the corresponding unmodified class IgG antibody wherein

(a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

42. (Previously presented) The modified antibody of Claim 39, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

43-51. (Canceled)

52. (Currently amended) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the modified antibody according to ~~Claim 2~~ Claim 1.

53. (Previously presented) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody according to Claim 20.

54. (Currently amended) A polypeptide comprising an amino acid sequence of ~~anyone of~~ SEQ ID NOs: [[10-76]] 13 or 23.

55-56. (Canceled)

57. (Currently Amended) A method for preparing an antibody of Claim 1, said method comprising substituting residues 250 and 428, EU numbering, in the heavy chain constant region with glutamic acid or glutamine at residue 250 and leucine or phenylalanine at residue 428 ~~amino acids different from those present in the unmodified antibody.~~

58 (Currently Amended) A method of producing a modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an altered binding affinity for FcRn and/or an altered serum half-life as compared with the unmodified antibody, said method comprising:

(a) preparing an expression vector comprising a suitable promoter operably linked to DNA encoding at least a variable region and a constant region of an immunoglobulin heavy chain in which residue 250 and 428, EU numbering, [[are]] is substituted with glutamic acid or glutamine and residue 428, EU numbering, is substituted with leucine or phenylalanine ~~a residue different from that present in an unmodified antibody;~~

(b) transforming host cells with said vector; and
(c) culturing said transformed host cells to produce said modified antibody.

59. (Original) The method according to Claim 58, further comprising: preparing a second expression vector comprising a promoter operably linked to DNA encoding a complementary immunoglobulin light chain and further transforming said host cells with said second expression vector.

60. (canceled)

61. (Previously presented) The method according to Claim 58, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine.

62. (Previously presented) The method according to Claim 58, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

63. (Previously presented) The method according to Claim 58, wherein

- (a) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with phenylalanine;
- (b) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with phenylalanine; or
- (c) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

64. (Previously presented) The method according to Claim 58, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

65-66. (Canceled)

67. (Currently amended) The method according to Claim 58, wherein said antibody of class IgG comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule:

~~—— (a) —— amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with a residue selected from a group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or~~

~~—— (b) —— amino acid residue 428, EU numbering, is substituted with a residue selected from the group consisting of alanine, arginine, asparagine, aspartic acid,~~

~~cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.~~

68. (Currently amended) The method according to Claim 58, wherein said antibody of class IgG comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with aspartic acid.

69. (Currently amended) The method according to ~~Claim 58~~ Claim 67, wherein said antibody of class IgG is a human class IgG1 antibody amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with glycine.

70. (New) The modified antibody according to Claim 8, wherein the unmodified antibody is

OST577-IgG2M3, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 2, 4, and 5, respectively, or

OST577-IgG1, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 3, 4, and 5, respectively.

71. (New) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the modified antibody according to Claim 8.

72. (New) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody according to Claim 15.

73. (New) The modified antibody according to Claim 8, wherein residue 250, EU numbering, from the heavy chain constant region is glutamic acid.

74. (New) The modified antibody according to Claim 8, wherein residue 250, EU numbering, from the heavy chain constant region is glutamine.

75. (New) A method for preparing an antibody of Claim 8, said method comprising substituting residue 250, EU numbering, in the heavy chain constant region with glutamic acid or glutamine.